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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/006,352	01/13/1998	REINER GENTZ	PF454	3633

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/006,352	Applicant(s) GENTZ ET AL.	
	Examiner Eileen B. O'Hara	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-159 and 285-305* is/are pending in the application.

4a) Of the above claim(s) *118-135* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-117,136-159 and 285-305* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *24-159 and 285-305* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 24-159 and 285-305 are pending in the instant application. Claims 45, 47, 50 and 53-55 have been amended and claims 19-23 and 160-284 have been canceled as requested by Applicant in Paper Number 18, filed Sept. 28, 2001.

Election/Restrictions

2. Applicant's election with traverse of a nucleic acid molecule comprising a polynucleotide sequence encoding amino acid residues 31-300 of SEQ ID NO: 2 is acknowledged. The traversal is on the ground(s) that even assuming that the amino acid sequences listed by the Examiner represented distinct or independent inventions, restriction remains improper unless it can be shown that the search and examination of the groups would entail a serious burden, and that the search of the nucleic acid encoding the full-length polypeptide of SEQ ID NO: 2 would provide all data necessary to examine each claimed sequence and accordingly, the search and examination of the instant nucleic acid sequences would not entail a serious burden. This is not found persuasive because a nucleic acid molecule comprising a nucleotide sequence encoding the small numbers of residues listed in claim 118 might be found in a different gene and would not necessarily be found in a search for the full-length sequence. However, this has been found persuasive as far as nucleic acids encoding amino acids 1-300, 2-300, 31-300 and 31-283 of SEQ ID NO: 2, and claims encompassing those nucleic acids have been rejoined.

Therefore, Claims 24-117, 136-159 and 285-305 are currently under examination.

Claims 118-135 are withdrawn as being drawn to a non-elected invention.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statements

3. The file wrapper and computer data indicates that an information disclosure statement was filed June 21, 2000, but both the list of references, and the references, are not in the file and cannot be found in the IDS storage location. The Examiner requests that this IDS be resubmitted to the USPTO for consideration. Additionally, the information disclosure statement that was submitted on June 22, 2001 is also missing. The list of references is in the case, but the references are not with the case and cannot be found. The Examiner requests that this IDS also be resubmitted and apologizes for the inconvenience.

Drawings

4. Figure 2 of the instant application are presented on two separate panels. 37 C.F.R. § 1.84(U)(1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, they must be identified by the same number followed by a capital letter. For example, the two sheets of drawings which are labeled " Figure 2" in the instant specification should be renumbered "Figures 2A and 2B". It is noted that the specification has been amended changing Fig. 2 to Figure 2A-B, but a substitute drawing for this figure has not been received. Substitute Figures 3 and 4 were received on June 13, 2001.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 24-117, 136-159 and 285-305 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 24-117, 136-159 and 285-305 are directed to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO: 1 or nucleic acids encoding the protein of SEQ ID NO: 2, identified as TNFR-6α. The instant specification discloses that TNFR-6α is a 300 amino acid protein, and provides sequence alignments with known tumor necrosis factor receptors (Fig. 3). The specification discloses that the amino acid sequence of TNFR-6α is about 23% similar to and shares multiple conserved cysteine rich domains with the translation product of the human TNFR-2 mRNA, and that this protein is a member of the tumor necrosis factor receptor family due to this structural homology and presence of conserved cysteine residues in the extracellular domain. Although the evidence is supportive of this protein being a receptor of the TNFR family, the protein does not have any specific and substantial utility, or a well established utility, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

The instant application describe the uses and methods of the invention, and state that the nucleic acids and proteins can be used in methods such as screening assays to identify ligands, binding proteins, agonists or antagonists, use of the protein as a molecular weight marker or to raise monoclonal or polyclonal antibodies, use of the nucleic acid to make fusion proteins or to identify chromosomes or location of particular sites on a chromosome, expressing the nucleic

acid in order to make the protein, or to determine tissue expression by Northern blotting, for example.

However, none of these uses are considered to be specific or substantial utilities for either the nucleic acid molecules or the protein encoded by them. Methods such as identification of ligands, use to screen for homologous genes, use to identify chromosomes or chromosomal location, use to recombinantly produce protein or use to generate antibodies are considered general methods applicable to any nucleic acid and/or protein, and are not considered specific or substantial.

The instant application also teaches that the nucleic acids, protein and associated antibodies, agonists, antagonists and antisense nucleic acids can be used either diagnostically to identify mutations, disorders or diseases, or therapeutically to treat diseases or disorders, such as those described on page 37 and including some immune system disorders as hypersensitivity, allergy, infectious disease, graft-host disease, immunodeficiency, autoimmune diseases and the like, and on page 39 other diseases such as cancers, AIDS, neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Retinitis pigmentosa among others, myelodysplastic syndromes such as aplastic anemia, ischemic injury such as caused by stroke or myocardial infarction, toxin-induced liver disease, septic shock, cachexia and anorexia.

However, the assertion that the nucleic acids/and or proteins of the instant invention can be used in the diagnosis or treatment of diseases or disorders is also not a specific and substantial utility, and is based on the assumption that the proteins are receptors in the tumor necrosis factor receptor family, which as a family are involved in myriad biological pathways and activities. Many proteins are members of evolutionarily related families, yet have diverse biological

activities and functions. Skolnick et al. (Trends in Biotechnology, 2000) teach that because proteins can have similar structures but different functions, determining the structure of a protein may not necessarily reveal its function (see entire article, especially Box 2.). On page 34, right column, fifth paragraph down, Skolnick et al. States:

"In addition, proteins can gain and lose function during evolution and may, indeed, have multiple functions in the cell (Box 1). Sequence-to-function methods cannot specifically identify these complexities. Inaccurate use of sequence-to-function methods has led to significant function-annotation errors in the sequence databases[17]."

Though sequence homologies may provide information as to the family a protein may belong to, they still do not necessarily predict a function. Even 99% homology does not allow predictability, as evidenced by Yan et al., which discloses a ligand (EDA) that is present in two forms (splice variants), the only difference being that one form has two extra amino acids. These two splice variants have completely different, non-overlapping specificities, and bind to two different receptors. Both are ligands and bind to receptors and therefore fall into the same class of protein, but the specific activity of one is not predictable from the specific activity of the other.

There is no nexus between any of the diseases or disorders and the molecules of the instant invention. Given no disease state or any other function or activity known for the proteins, the proteins are not considered to have utility. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds

are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a polynucleotide encoding a protein which has undetermined function or biological significance, and the use of an orphan receptor to discover its ligand or properties does not constitute a specific, substantial utility. All of the biological activities of a protein need not be known to obtain a patent, but there must be some specific and substantial activity or function known. It is possible that after further characterization, this protein might be found to have a patentable utility, in which case the polynucleotides encoding the protein would have a specific utility, or the polynucleotides might be found to be associated with a specific disease. This further characterization, however, is part of the act of invention, and until it has been undertaken the Applicants' claimed invention is incomplete. Because there is no specific and substantial utility asserted, credibility cannot be assessed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6.1 Claims 24-117, 136-159 and 285-305 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification

were enabling of how to use the TNFR-6α nucleic acid or polypeptide, enablement would not be found commensurate in scope with the claims. If one of skill in the art does not know how to use the nucleic acids or proteins the skilled artisan would clearly not know how to use nucleic acids that are 90-95% identical to the nucleic acid of SEQ ID NO: 1 or the cDNA of clone HPHAE52, or nucleic acids that encode a protein that is 90-95% identical to the protein of SEQ ID NO: 2 or the protein encoded by the cDNA of clone HPHAE52.

6.2 The enablement of claims 56-87, 104-117 and 148-159 requires availability of the specific sequence claimed therein. This determination has been made because said cDNA clone is not fully disclosed nor has it been shown to be publicly known and freely available. Accordingly, it is deemed that a deposit of the cDNA clone HPHAE52 deposited as ATCC Deposit Number 97810 should have been made in accordance with MPEP Chapter 2400 and 37 C.F.R. §§ 1.801-1.809.

Applicant, their assignee or their agent needs to provide a declaration containing the following:

The identification of the declarant.

A statement that a deposit has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.

A statement that the deposited material has been accorded a specific, recited, accession number.

A statement that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122.

A statement that the deposited material will be maintained with all of the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty years after the date of deposit or for the enforceable life of the patent, whichever period is longer.

A statement by declarant that all statement made therein of declarant's knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternately, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent. Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession number) number, name and address of the depository, and the complete taxonomic description.

Conclusion

7. No claims are allowed.

The art considered pertinent to the present application is U.S. Patent No. 5,885,800, which discloses a polynucleotide that is 100% identical to the polynucleotide of SEQ ID NO:1 and that encodes a polypeptide identical to the polypeptide of SEQ ID NO: 2 of the present application. This is not considered prior art, since the provisional application of the instant application was filed before the application of the patent was filed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242.

Informal papers filed by fax should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER